

***Remarks***

Applicants respectfully request the Examiner enter the Supplemental Amendment which is being submitted herewith in response to the Interview conduct on July 20, 2007. Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 215, 216, 219, 221-232, 235, 237-246, 249, 251-262, 265, 267-276, 279, 281-296 are pending in the application, with claims 215, 245, 261 and 275 being the independent claims. Claims 217, 218, 233, 234, 247, 248, 263 and 264 are sought to be canceled without prejudice to or disclaimer of the subject matter therein. New claims 293-296 have been added to specifically recite the route of administration.

These changes are believed to introduce no new matter, and their entry is respectfully requested. Support for the amendment to the claims 215, 231 and 275 adding the limitation "30 to 764" is found in the originally filed claims. Support for the amendment to claims 215 and 245 adding the limitations "prophylactically vaccinate" and "prophylactically effective immune response" is found, in the specification, *inter alia*, at paragraphs [0014], [0121], [0122], [0133], [0169] and in Example 13. Support for new claims 293-296 reciting a specific route of administration is found, in the specification, *inter alia*, in Example 13 of the specification. Accordingly, no new matter has been added by these amendments.

Based on the above amendment, the previously presented remarks and arguments submitted in the Amendment and Reply filed June 5, 2007, in conjunction with the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Statement of Substance of Interview***

Pursuant to 37 C.F.R. § 1.133, Applicants provide the following statement of Substance of the Interview. Applicants wish to thank Examiner Anoop Singh, Ph.D. and Examiner Anne-Marie Falk, Ph.D. for the courtesy of an interview with Applicants' representatives on July 20, 2007. Rejections of record and proposed claim amendments were discussed. Amendments, as discussed, are filed herewith.

***Pending Claims***

The claims have been amended in view of the discussion during the interview of July 20, 2007. The following is a summary of the claim amendments:

Claims 215, 231 and 275 have been amended to recite a nucleic acid fragment which encodes a polypeptide at least 97% identical to amino acids 30 to 764 of SEQ ID NO:4, wherein the nucleic acids encoding the amino acids corresponding to the furin cleavage site have been deleted. Therefore, the independent claims 215, 231, 245, 261 and 275 are now directed to the same nucleic acid fragment.

Claims 217, 218, 233, 234, 247, 248, 263, 264 have been canceled.

Additionally, claims 215, 231, 245, 261 have been amended to include a resolution step that reads back on the preamble of the claim.

Claims 215, 216, 219, 221-232, 235, 237-244, 293 and 294 are directed to methods using a composition comprising GAP-DMORIE, a co-lipid and an isolated polynucleotide.

Claims 245, 246, 249, 251-262, 265, 267-274, 295, 296 are directed to methods using compositions comprising DMRIE, a co-lipid and an isolated polynucleotide.

Claims 275, 276, 279, 281-292 are directed to a composition.

***Rejections under 35 U.S.C. § 112***

***35 U.S.C. § 112, first paragraph (scope of enablement)***

The Examiner has rejected claims 215-292 under 35 U.S.C. § 112, first paragraph. (OA at pages 2.) The Examiner asserts that the specification while "being enabling to reduce the severity of anthrax infection" in a mammal, does not reasonably provide enablement for a method of "preventing anthrax infection." (OA at pages 3, line 5.) Applicants respectfully traverse this rejection for the reason set out in the Amendment and Reply June 5, 2007, and incorporated herein in its entirety. The following remarks solely address the outstanding issues and concerns raised during the interview of July 20, 2007.

***i. prevention / cure***

The Examiner asserts there is enablement in the specification for the limitation "to reduce the severity of anthrax" (OA at page 2) but not sufficient enablement for a method of "preventing anthrax infection." (OA at page 3, line 5.) Further, the Examiner asserts that the definition of "treatment of a vertebrate" provided in the specification included prevention, cure, retard or reduce the severity of anthrax. Specifically, the

Examiner has asserted that the definition provided in the specification encompasses "cure" which allegedly is not enabled by the specification. (OA at page 4.)

Applicants respectfully disagree with the Examiner's position. However, solely in an effort to advance prosecution, and not in acquiescence to any reasoning underlying the Examiner's rejection claims 215 and 245 have been amended to omit the phrase "prevent anthrax infection" and substitute therefore the phrase "prophylactically vaccinate a vertebrate against anthrax infection." The amendment should obviate the Examiner's rejection, thereby rendering the Examiner's rejection moot.

Applicants have enabled the present invention directed to prophylactically vaccinating a vertebrate against anthrax infection. Specifically, in example 13 of the specification Applicants have protected rabbits from a lethal anthrax challenge. Example 13 provides a working example of a prophylactic vaccination using the presently claimed methods and composition. Here, the rabbits were injected with the composition on days 0, 28 and 56; the rabbits were subsequently challenged using a lethal dose of aerosolized anthrax spores on day 70; the rabbits were then observed for an additional 19-22 days after the exposure to the challenge dose. All rabbits that received the vaccine survived, while those that did not receive the vaccine perished. (*See* Table 17.) Therefore, Applicants have enabled the method of prophylactically vaccinating a vertebrate as recited in the presently-pending claims. Reconsideration and withdrawal of this rejection is respectfully requested.

***ii. administration via any route***

The Examiner alleges that it would require extensive experimentation to carry out the claimed method. (OA at pages 7.) Specifically, the Examiner asserts the

specification or cited art "does not provide any evidence that compositions comprising (GAP-DMORIE) and any co-lipid administered via any route would elicit immune response to a level sufficient to reduce severity of anthrax infection as exemplified in the instant application." (OA at page 6) (emphasis added) The Examiner appears to doubt whether the ordinary artisan would be able to prophylactically vaccinate or to lessen the severity of anthrax by administering the vaccine using a route of administration not exemplified in the specification. Applicants respectfully traverse this rejection.

During the interview the Examiner indicated that a showing of other successful DNA vaccines formulated with either Vaxfectin<sup>TM</sup> or DMRIE, plus a co-lipid using other administration routes might be persuasive on this point of enablement. At the very least, the Examiner indicated that he would at least consider the additional references.

DNA vaccines mixed with Vaxfectin<sup>TM</sup> can be successfully delivered via multiple delivery routes and elicit an effective immune response. For example, measles DNA formulated with Vaxfectin<sup>TM</sup> and administered via intradermal or intramuscular routes produced sterilizing immunity in monkeys. Furthermore, there was no difference noted between the route of injection and the level of immunity. (*See* Exhibit 1)

HIV-2 env DNA mixed with Vaxfectin<sup>TM</sup> and administered to mice produced a superior immune response when compared to conventional methods or administration. The mice produced a gp140-specific immune response with either intramuscular, intradermal or intranasal administration. Interestingly the systemic antibody response where highest with the intradermal administration, while the mucosal immune response was highest using the intramuscular administration. (*See* Exhibit 2)

Delivery of DNA to the submandibular gland also results in antibody production. Rats that were administered DNA encoding influenza NP protein complexed with Vaxfectin<sup>TM</sup> produced an immune response to the protein encoded by the DNA. Specifically, this route of immunization produced IgG subclass stimulation, while it did not produce an IgA response. (See Exhibit 3.)

Vaxfectin<sup>TM</sup> DNA compositions have been shown to increase antibody production when compared to DNA in saline. Using Vaxfectin<sup>TM</sup> in combination with a DNA encoding *Mycobacterium tuberculosis* antigen 85A produced 10 fold higher antibody titers in inoculated mice. (See Exhibit 4.)

Additionally, DNA formulated with Vaxfectin<sup>TM</sup> also produced a long lasting immune response. A CMV vaccine formulated with Vaxfectin<sup>TM</sup> produces a long lasting memory cell response. (See Exhibit 5.)

Furthermore, DNA administration to a mucosal surface has been shown to produce a cell mediated and antibody mediated response on other mucosal surfaces. Intranasal immunization of a DNA complexed with DMRIE/DOPE results in a general mucosal response. This combination is effective at eliciting an antigen specific CTL response as well as producing an IgA response at a distant site, the genital and rectal tract, from the site of inoculation, the nares. Thus, this formulation provides an attractive non-invasive route of administering DNA to a vertebrate.

Therefore, the Exhibits show that the use of DNA formulated with Vaxfectin<sup>TM</sup> or DMRIE plus a co-lipid will elicit a sufficient immune response using a variety of administration routes. The Examiner is reminded that all that is necessary for enablement is that one skilled in the art be able to practice the claimed invention, given

the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. *See, e.g., In re Fisher*, 427 F.2d 833, 839 (CCPA 1970). *See* MPEP 2164.08. Applicants submit that the specification has provided sufficient teaching, as well as an actual reduction practice of the claimed invention to enable the ordinary artisan in the vaccine field to practice the full scope of the invention as presently-claimed. Applicants respectfully request reconsideration and withdrawal of this rejection.

***iii. effective immune response with 97% identity to SEQ ID NO:4***

Applicant thanks the Examiner for withdrawing this part of the rejection. (OA at page 5.)

***iv. DNA delivery***

The Examiner asserts that the specification does not provide "any evidence that a composition comprising (GAP-DMORIE) and any co-lipid administered via any route would elicit immune response to a level sufficient to reduce severity of anthrax infection as exemplified in the instant application." (OA at page 6.) The Examiner asserts that there is a need for an "optimal immune response" for the prevention or reduction of severity of anthrax infection." (OA at page 6.) Applicant respectfully traverses this rejection.

For the reasons set out above, Applicants assert that the varying routes of administration of a DNA vaccine are enabled for producing an immune response in a vaccinated animals. (*See* Exhibits 1-6)

***Rejections under 35 U.S.C. § 103***

The Examiner has rejected claims 215-292 under 35 U.S.C. § 103(a) as being unpatentable over Lee *et al.* (U.S. Pat. App. No. 2004/0009945, publication date January 15, 2004, effective filing date July 10, 1998); Nagata *et al.* (Biochemical Biophysical Research Comm. 1999, Vol. 261, No. 2, pages 445-451; hereinafter "Nagata") and Hartikka *et al.* (Vaccine 2001, Vol. 19, pages 1911-1923; hereinafter "Hartikka"). (OA at pages 9.)

For the reason set out in the Amendment and Reply June 5, 2007, and incorporated herein in its entirety, the combined references cited by the Examiner do not suggest the claimed methods, and specifically claimed molecular modifications. Accordingly, Applicants respectfully assert that a *prima facie* case of obviousness has not been established because all the elements are not present in the references. Applicant respectfully requests withdrawal of the rejection as it relates to the currently pending claims.

During the Interview the Examiner suggested that the claim amendments of June 5, 2007, directed to the deletion of the furin cleavage site from the polynucleotide construct appear to have overcome the rejection based on the presently cited references. The Examiner did indicate that another search of the art will be conducted.

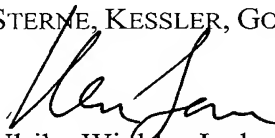
***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Ulrike Winkler Jenks  
Attorney for Applicant  
Registration No. 59,044

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1100 New York Avenue, N.W.  
Washington, D.C. 20005-3934  
(202) 371-2600  
701394\_1.DOC